HRCT features of interstitial lung disease in dermatomyositis with anti-CADM-140 antibody.

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Title: HRCT FEATURES OF INTERSTITIAL LUNG DISEASE IN DERMATOMYOSITIS WITH ANTI-CADM-140 ANTIBODY

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1 **Running title:** HRCT in DM-ILD with anti-CADM-140

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Abstract

Background: Anti-CADM-140 antibody (anti-CADM-140), also referred to as anti-melanoma differentiation-associated gene 5 (MDA5) antibody, is a myositis-specific antibody identified in the sera of patients with clinically amyopathic dermatomyositis (C-ADM) and is associated with a worse prognosis in dermatomyositis-associated interstitial lung disease (DM-ILD). We sought to determine high-resolution computed tomography (HRCT) features of DM-ILD with anti-CADM-140.

Methods: Twenty-five patients newly diagnosed with DM-ILD at Kyoto University Hospital between 2005 and 2009 were retrospectively reviewed. Serum anti-CADM-140 was measured in all patients at their first visit. Chest HRCT images taken prior to treatment were classified based on the dominant findings and their distribution, and compared between patients with and without the antibody.

Results: Of 25 DM-ILD patients, 12 were positive and 13 were negative for anti-CADM-140. HRCT patterns differed significantly between anti-CADM-140-positive and negative patients ($P = 0.002$). Lower consolidation or ground-glass attenuation (GGA) pattern (50.0%) and random GGA pattern (33.3%) were the predominant patterns in anti-CADM-140-positive cases, while lower reticulation pattern (69.2%) was frequently seen in anti-CADM-140-negative cases. Anti-CADM-140-positive cases were also significantly characterized by the absence of intralobular reticular opacities (0% in anti-CADM-140 (+) vs. 84.6% in anti-CADM-140 (-), $P < 0.0001$).

Conclusions: Anti-CADM-140-positive DM-ILD was characterized by lower consolidation or GGA pattern, random GGA pattern, and the absence of intralobular reticular opacities.

Keywords: amyopathic dermatomyositis; anti-CADM-140 antibody; interstitial lung disease; high-resolution computed tomography

Introduction

Interstitial lung disease (ILD) is observed in 5-65% of polymyositis (PM) and dermatomyositis (DM) cases,[1 2] and is a significant prognostic factor.[1] PM/DM-associated ILD (PM/DM-ILD) can be divided into acute and chronic types.[3] The acute type of PM/DM-ILD is often rapidly progressive and refractory to treatment, resulting in fatal outcome.[3]

PM and DM are also characterized by several serum autoantibodies specific to PM/DM, designated as myositis-specific antibodies (MSAs).[4] Anti-CADM-140 antibody (anti-CADM-140) was the MSA identified in 2005 by Sato and coworkers in the sera of patients with clinically amyopathic dermatomyositis (C-ADM).[5] It recognizes interferon (IFN)-induced with helicase C domain protein 1/melanoma differentiation-associated gene 5 (IFIH1/MDA5)[6] and is thus also referred to as anti-MDA5 antibody.[7] It is specific to DM and is associated with the acute type of DM-ILD.[6 7] As expected from these findings, anti-CADM-140 was reported to be associated with a worse prognosis in patients with DM-ILD, compared to anti-aminoacyl-tRNA synthetase (ARS) antibodies (anti-ARS).[7] On the other hand, acute and chronic types of DM-ILD were shown to display different radiological features.[3] However, the radiological features of DM-ILD with anti-CADM-140 or the relationships between anti-CADM-140 and radiological findings have not been elucidated thus far.

In the present study, we aimed to define high-resolution computed tomography (HRCT) features of DM-ILD with anti-CADM-140. We compared HRCT findings between anti-CADM-140-positive and negative DM-ILD cases, and investigated

whether the HRCT features could discriminate between the antibody-positive and negative cases.

Methods

Patients

The study population included all patients who were diagnosed with DM at Kyoto University Hospital between 2005 and 2009. DM was diagnosed using the Bohan and Peter criteria.[8] C-ADM was diagnosed if a patient had the characteristic skin rash of DM but little or no muscle symptoms and serum creatine kinase (CK) was <300 IU/L during the study period, as described previously.[5,6] We excluded patients who had active neoplasm or other connective tissue disease (CTD), or had been treated with systemic corticosteroid (CS) or immunosuppressive agents before referral to our hospital. Among the remaining 32 patients, ILD was confirmed in 25 (78.1%) based on HRCT. Acute and subacute DM-ILD subtypes were diagnosed when respiratory failure developed within 1 month and within 1 to 3 months, respectively, from the onset of symptoms or the initiation of treatment.

All patients provided written informed consent before blood sample collection. The Kyoto University Hospital Institutional Review Board approved this retrospective study.

Clinical evaluation

Clinical information was retrospectively collected from medical records. All

patients were evaluated by at least two rheumatologists prior to treatment and had blood tests at their first visit. Most patients also underwent standardized pulmonary function tests,[9] and arterial blood gas analysis was done before treatment. Published equations for Japanese adults were used to determine predicted values of each parameter.[10]

Measurement of MSAs

Serum samples were obtained from all patients at the first visit prior to receiving immunosuppressive therapies. The presence of MSAs was determined by RNA-immunoprecipitation (RNA-IPP) for anti-ARS and protein-immunoprecipitation (P-IPP) for anti-CADM-140 as described previously.[6] Patients were divided into two groups based on the presence or absence of anti-CADM-140: anti-CADM-140 (+) or (-), respectively.

HRCT scanning protocol

Thin-section CT images were obtained with a multi-detector CT scanner (Aquilion 64; Toshiba Medical Systems, Tochigi, Japan). Whole lung scans were performed at peak tube voltage of 120 kVp with variable mAs setting using an automatic exposure control system (SD value 8.5). Contiguous 7-mm-thick images and HRCT images (2 mm) were prepared for review.

HRCT evaluation

All patients underwent chest HRCT prior to treatment, and images were

reviewed by three independent observers (T.K., T.H., and K.T. with 15, 12, and 10 years of experience, respectively) blinded to clinical information. Inter-observer disagreements were resolved by consensus.

Images were assessed for the presence of ground-glass attenuation (GGA), consolidation, intralobular reticular opacities, interlobular septal thickening, non-septal linear or plate-like opacity, substantial micronodules, honeycombing, emphysema, traction bronchiectasis, and lobar volume loss. The presence of mediastinal lymph node enlargement or pleural effusion and the laterality of abnormalities were also assessed. HRCT findings were interpreted according to the recommendations of the Nomenclature Committee of the Fleischner Society.[11] Nonseptal linear or plate-like opacity was defined as an elongated line of soft tissue attenuation that was distinct from interlobular septa and bronchovascular bundles, including subpleural curvilinear lines and subpleural bands.[12]

Through reviewing all HRCT images, we found that all 25 cases could be categorized into a few HRCT patterns, based on dominant CT findings, and the craniocaudal and axial distribution of these findings. The dominant findings were classified as GGA, consolidation, or reticulation (intralobular reticular opacities, interlobular septal thickening, or nonseptal linear or plate-like opacity). The craniocaudal distribution was assessed as upper, lower, diffuse, or random. Upper distribution was defined as extensive findings predominantly above the level of inferior pulmonary veins, lower when there were more below this level, diffuse when generalized, and random for no zonal predominance. The axial distribution was

classified as peribronchovascular when the dominant findings were along the bronchi and vessels, peripheral when in the outer one-third of the lung, diffuse when generalized, or random when no distribution pattern was apparent.

Statistical analysis

Statistical analysis was performed using JMP ® version 6 (SAS Institute Inc. Cary, NC, USA). All statistical variations in quantitative data were expressed as a single determination standard deviation, and a *P* value less than 0.05 was considered to indicate statistical significance.

Group comparisons were made using Fisher's exact test, χ^2 test, and Mann-Whitney U test. Cumulative survival probabilities were estimated using the Kaplan-Meier method and the log-rank test.

Results

Initial clinical features

Demographics, clinical manifestations and laboratory test results of patients in the anti-CADM-140 (+) and (-) groups are summarized in Table 1. The prevalence of C-ADM showed no significant difference (50.0% vs. 30.8%, $P = 0.43$). Acute DM-ILD was diagnosed in 25% of patients in the anti-CADM-140 (+), and 0% of patients in the anti-CADM-140 (-) group ($P = 0.10$), while the sum of acute and subacute subtypes was 41.7% and 7.7%, respectively ($P = 0.07$). Before treatment, white blood cells, platelets, CK, and aldolase levels were lower in the anti-CADM-140 (+) group. Pretreatment

ferritin and its maximal value were both higher in the anti-CADM-140 (+) group. In the anti-CADM-140 (-) group, 10 patients (76.9%) were positive for anti-ARS: three with EJ, three with PL-7, two with Jo-1, one with OJ, and one with PL-12. Arterial blood gas analyses and pulmonary functional tests revealed no significant differences (data not shown). No patients underwent surgical lung biopsy (SLB) in either group.

HRCT evaluation

HRCT findings are shown in Table 2. Common findings were GGA (83.3%), nonseptal linear or plate-like opacity (83.3%), and interlobular septal thickening (66.7%) in the anti-CADM-140 (+) group; and GGA (100.0%), intralobular reticular opacities (84.6%), non-septal linear or plate-like opacity (53.8%), and lobular volume loss (53.8%) in the anti-CADM-140 (-) group. Among the HRCT findings, intralobular reticular opacities were significantly different between the groups (0% in anti-CADM-140 (+) vs. 84.6% in anti-CADM-140 (-), $P < 0.0001$).

Next, we categorized all 25 cases into four HRCT patterns: lower consolidation/GGA pattern (lower peripheral or peribronchovascular consolidations or GGA); lower reticulation pattern (lower peripheral or peribronchovascular reticulation); random GGA pattern (random peripheral GGA); and others. Lower consolidation/GGA pattern was characterized by nonsegmental consolidations or GGA, with subpleural or peribronchovascular distribution (Figs. 1 and 2). Lower reticulation pattern showed a homogeneous distribution with some subpleural sparing (Fig. 3). In random GGA pattern, small GGAs were seen in a patchy manner in the absence of consolidation (Fig.

4).

The HRCT patterns were significantly different between the anti-CADM-140 (+) and (-) groups (P = 0.002): with lower consolidation/GGA pattern (50.0%) and random GGA pattern (33.3%) in the anti-CADM-140 (+) group, and lower reticulation pattern (69.2%) in the anti-CADM-140 (-) group. Additionally, the dominant abnormalities were seen in lower lung fields (6/12, 50%) or randomly (4/12, 33.3%) in anti-CADM-140-positive patients, compared to lower lung fields (12/13, 93.2%) in most anti-CADM-140-negative patients (P = 0.04). The HRCT patterns in the seven fatal anti-CADM-140 (+) cases were lower consolidation/GGA pattern in four, random GGA pattern in two (including the one patient who died of *Pneumocystis jiveroci* pneumonia and sepsis), and others in one (Table 3). Of 10 patients with anti-ARS antibodies in the anti-CADM-140 (-) group, six (60.0%) had a lower reticulation pattern and two (20.0%) had lower consolidation/GGA pattern. Three patients who were negative for both anti-CADM-140 and anti-ARS showed lower reticulation pattern.

Treatment and outcome

All patients received corticosteroid (CS) therapy, and immunosuppressive (IS) agents; most commonly cyclosporine A (CsA), used in 83.3% and 69.2% in the anti-CADM-140 (+) and (-) groups, respectively.

The median follow-up period from the diagnosis of DM for all patients was 588 days (range, 41-1617 days). Of 12 patients in the anti-CADM-140 (+) group, seven died and five survived, while all 13 patients in the anti-CADM-140 (-) group survived (P <

0.01). Of the seven deaths in anti-CADM-140 (+) group, five patients died of progressive ILD that was refractory to initial treatment. The remaining two patients died after the disease had been well controlled for months. One patient died of *Pneumocystis jiroveci* pneumonia and sepsis, and another of acute exacerbation of ILD without infection. All seven patients were treated with corticosteroids and CsA, whereas cyclophosphamide (CYC) was used in six patients.

Discussion

We demonstrated that radiological features of anti-CADM-140-positive DM-ILD were significantly different from those of anti-CADM-140-negative cases, based on the original classification of HRCT patterns. In our series, anti-CADM-140-positive DM-ILD was characterized by lower consolidation/GGA and random GGA pattern and the absence of intralobular reticular opacities. To our knowledge, this is the first report describing HRCT features of DM-ILD with anti-CADM-140 in comparison with DM-ILD without this antibody.

The HRCT patterns characterized by the dominant findings and the distributions of such abnormalities were significantly different between the anti-CADM-140 (+) and (-) groups. Lower consolidation/GGA and random GGA patterns predominated in the anti-CADM-140 (+) group, while lower reticulation was more common in the anti-CADM-140 (-) group. Lower reticulation pattern is consistent with idiopathic nonspecific interstitial pneumonia (NSIP)[13-15] and DM/PM-ILD having biopsy-proven NSIP pattern:[16] reticulation, GGAs, lobar volume loss, and lower predominance, but

little or no honeycombing. More than half of the anti-CADM-140-negative patients (69.2%, including six anti-ARS positive patients) in our series had this pattern, suggestive of pathological NSIP pattern. On the other hand, lower consolidation/GGA and random GGA patterns are more difficult to interpret. Lower consolidation/GGA pattern may indicate organized pneumonia (OP)[14 17] or localized diffuse alveolar damage (DAD).[14 17-19] The mortality in patients with this pattern was as high as 50.0% (4/8), suggesting a high prevalence of DAD although radiopathological correlation was not confirmed in our cases. Indeed, Kang et al. reported biopsy-proven DAD, usual interstitial pneumonia (UIP), and NSIP patterns in DM-ILD, while HRCT findings showed OP pattern in most cases.[20] In random GGA pattern, most lesions were too small to speculate pathology.

Another significant characteristic of anti-CADM-140-positive DM-ILD was the absence of intralobular reticular opacities. Intralobular reticular opacities represent abnormal thickening of intralobular interstitial tissue[11] and were observed in 87% of idiopathic NSIP patients[13] and 92% of DM/PM-ILD patients with biopsy-proven NSIP pattern.[16] Thus, the absence of lower reticulation pattern and intralobular reticular opacities in the anti-CADM-140 (+) group indicates a lower prevalence of pathological NSIP pattern among anti-CADM-140-positive cases, in contrast to anti-CADM-140-negative cases. Additionally, the reported responses to treatment and outcomes of DM/PM-ILD patients with biopsy-proven NSIP pattern were much better than those of our anti-CADM-140-positive patients.[16] Although the prognostic value of pathology in DM-ILD have not been established, these differences in both radiological

findings and survival suggest that the anti-CADM-140 (+) group includes patients distinct from those with pathological NSIP.

On the other hand, HRCT findings other than intralobular reticular opacities were not significantly different between the anti-CADM-140 (+) and (-) groups. Our results indicate that HRCT patterns may be more helpful in discriminating between anti-CADM-140-positive and negative cases than several nonspecific findings. The HRCT patterns in our study were based on the major abnormalities and the distributions of those abnormalities to describe the overall picture comprehensively and concisely. Thus, the complete picture of HRCT images, rather than the presence of individual abnormalities probably characterized anti-CADM-140-positive cases better.

Among MSAs, anti-ARS has also been reported to be associated with ILD in DM/PM patients.[21] Of 13 anti-CADM-140 negative cases in our study, 10 were positive for anti-ARS, and the HRCT patterns were similar between anti-ARS-positive and negative cases: lower reticulation pattern was predominant (60.0% and 40.0% in anti-ARS-positive and negative patients, respectively). These findings indicate that anti-CADM-140 may be more influential on the HRCT patterns of DM-ILD than anti-ARS.

Notably, the prevalence of C-ADM was not significantly different between anti-CADM-140 (+) and (-) groups. In spite of the designation, half the patients in the anti-CADM-140 (+) group did not fulfill the criteria for C-ADM. Such a discrepancy between anti-CADM-140 and C-ADM was also suggested by Gono and coworkers.[7] In addition, the results of pulmonary function tests and arterial gas analyses

at diagnosis were not significantly different. These findings indicate that, while this antibody is a strong predictor of mortality, the initial clinical data cannot necessarily discriminate between anti-CADM-140-positive and negative cases in DM-ILD. In contrast, the HRCT features were significantly different between the two groups, suggesting the clinical utility of HRCT evaluation for predicting the presence of anti-CADM-140.

High mortality in the anti-CADM-140 (+) group suggested the necessity of novel therapies beyond the combination of corticosteroids and immunosuppressive agents, mainly CsA and/or CYC. On the other hand, approximately half of patients with anti-CADM-140 (41.7%) survived with current regimens. Table 3 suggests that the HRCT patterns may not be associated with survival in anti-CADM-140-positive DM-ILD; thus, the prognostic value of HRCT features at diagnosis is the next critical question. A recent study reported the prognostic value of serum ferritin in DM-ILD with anti-CADM-140, although the study population was relatively small.[7] Thus, the predictors of mortality in anti-CADM-140 positive DM-ILD, including HRCT features should be elucidated by analyzing larger numbers of patients. In addition, in the entire spectrum of DM-ILD, the prognostic values of HRCT features should also be compared to that of anti-CADM-140 and other serum biomarkers. As Goh et al. showed in systemic sclerosis-associated ILD[22], quantitative scoring of disease extent may be helpful in these analyses.

We should mention some limitations of this study. First, this study was a small-sized study in a single center. Second, serial changes in HRCT images were not

addressed because follow-up HRCT was performed at rather arbitrary intervals. The effects of treatment on HRCT features and their prognostic values should be further studied in a prospective design. Third, radiopathological correlation was not confirmed. However, the significance of pathological diagnosis or SLB in clinical practice of DM-ILD or CVD-related ILD has not been determined.[23 24] Further, SLB can sometimes induce acute exacerbation in idiopathic pulmonary fibrosis and other ILD patients.[25-27] Fourth, anti-CADM-140 has been reported exclusively in Japanese patients thus far.[5-7] To establish the clinical relevance of this antibody, further studies in other ethnic populations are required.

Despite these limitations, we demonstrated that lower consolidation/GGA pattern and random GGA patterns as well as the absence of intralobular reticular opacities were characteristic of anti-CADM-140-positive DM-ILD. Although HRCT evaluation can be useful in predicting the presence of anti-CADM-140 in DM-ILD, further studies are required to define the prognostic value of HRCT features in anti-CADM-140-positive DM-ILD.

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Conflicts of Interest

Kiminobu Tanizawa has no conflicts of interest to disclose. Tomohiro Handa has no conflicts of interest to disclose. Ran Nakashima has no conflicts of interest to disclose. Takeshi Kubo has no conflicts of interest to disclose. Yuji Hosono has no conflicts of interest to disclose. Kizuku Watanabe has no conflicts of interest to disclose. Kensaku Aihara has no conflicts of interest to disclose. Toru Oga has no conflicts of interest to disclose. Kazuo Chin has no conflicts of interest to disclose. Sonoko Nagai has no conflicts of interest to disclose. Tsuneyo Mimori has no conflicts of interest to disclose. Michiaki Mishima has no conflicts of interest to disclose.

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Figure legends

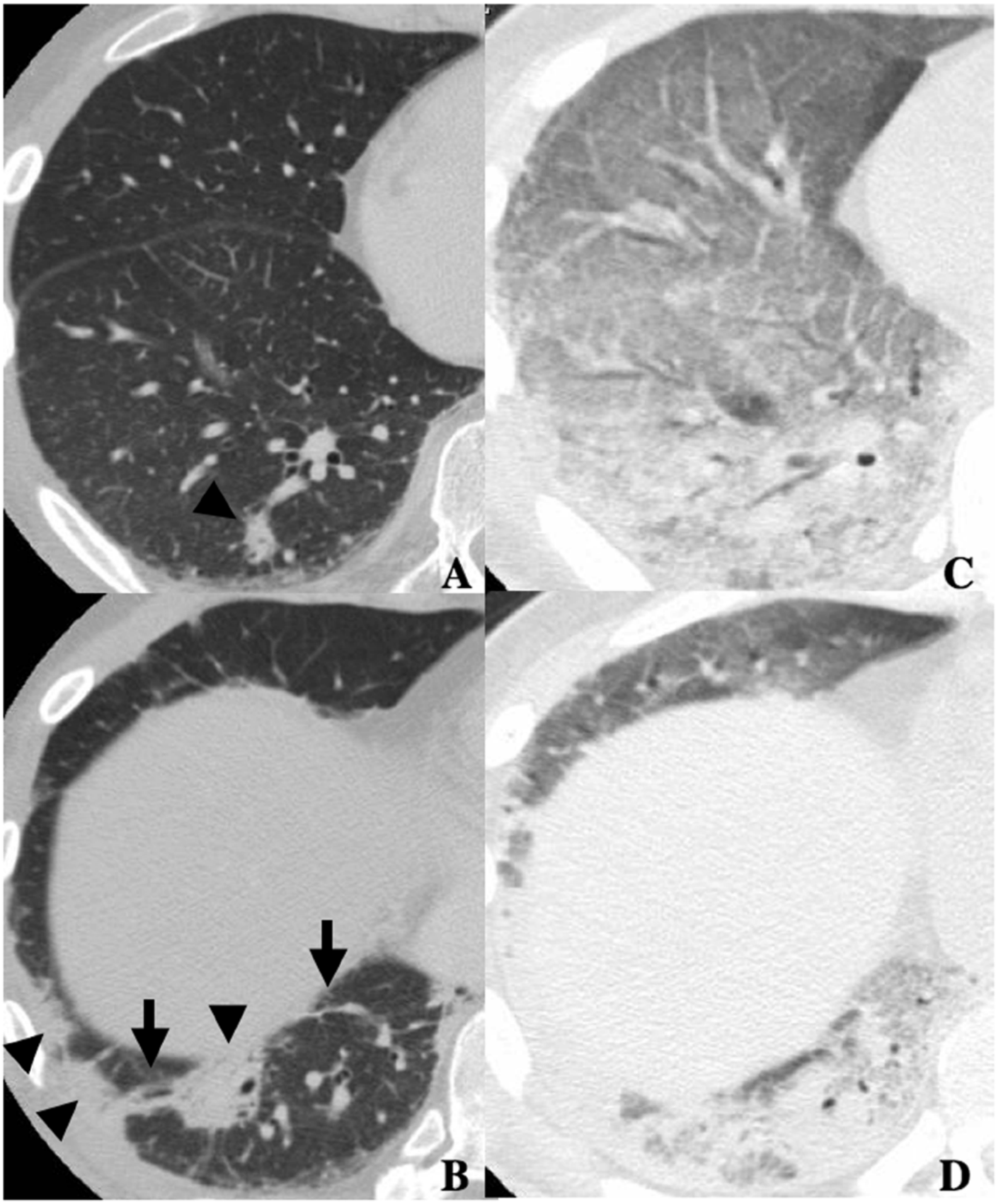
Figure 1. High resolution computed tomography (HRCT) images showing lower consolidation/ ground-glass attenuation (GGA) pattern in a 44-year-old man positive for anti-CADM-140 antibody (anti-CADM-140). A and B: At diagnosis, peripheral and peribronchovascular consolidations were observed (arrowheads). Interlobular septal thickening and nonseptal linear or plate-like opacities were also seen (arrows). C and D: Despite treatment for 6 weeks, severe respiratory failure developed, requiring mechanical ventilation. Diffuse GGA and consolidation with air bronchograms were extended in the whole lungs. Surveillance at this point revealed no evidence of infection. The patient died of respiratory failure 1 week later.

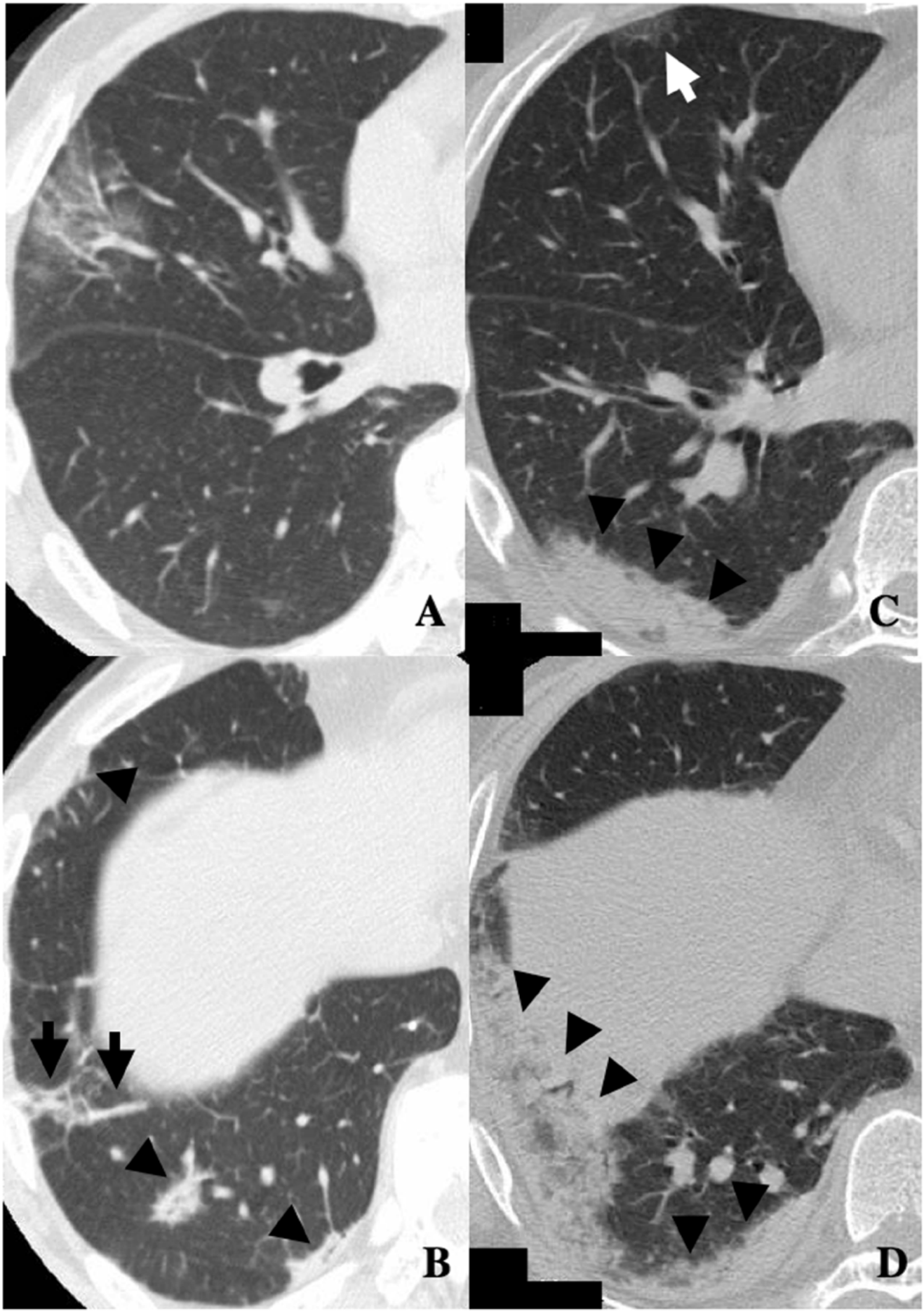
Figure 2. A and B: HRCT images showing lower consolidation/GGA pattern in a 51-year-old man positive for anti-CADM-140. A: At diagnosis, subpleural nonsegmental GGA was observed. B: Peripheral and peribronchovascular consolidations (arrowheads), and interlobular septal thickening and nonseptal linear or plate-like opacities (arrow) were also seen. C and D: HRCT images showing lower consolidation/GGA pattern in a 60-year-old man positive for anti-CADM-140. Subpleural nonsegmental consolidations with air bronchograms were observed (arrowheads). Subpleural nonsegmental GGA was also seen (arrow).

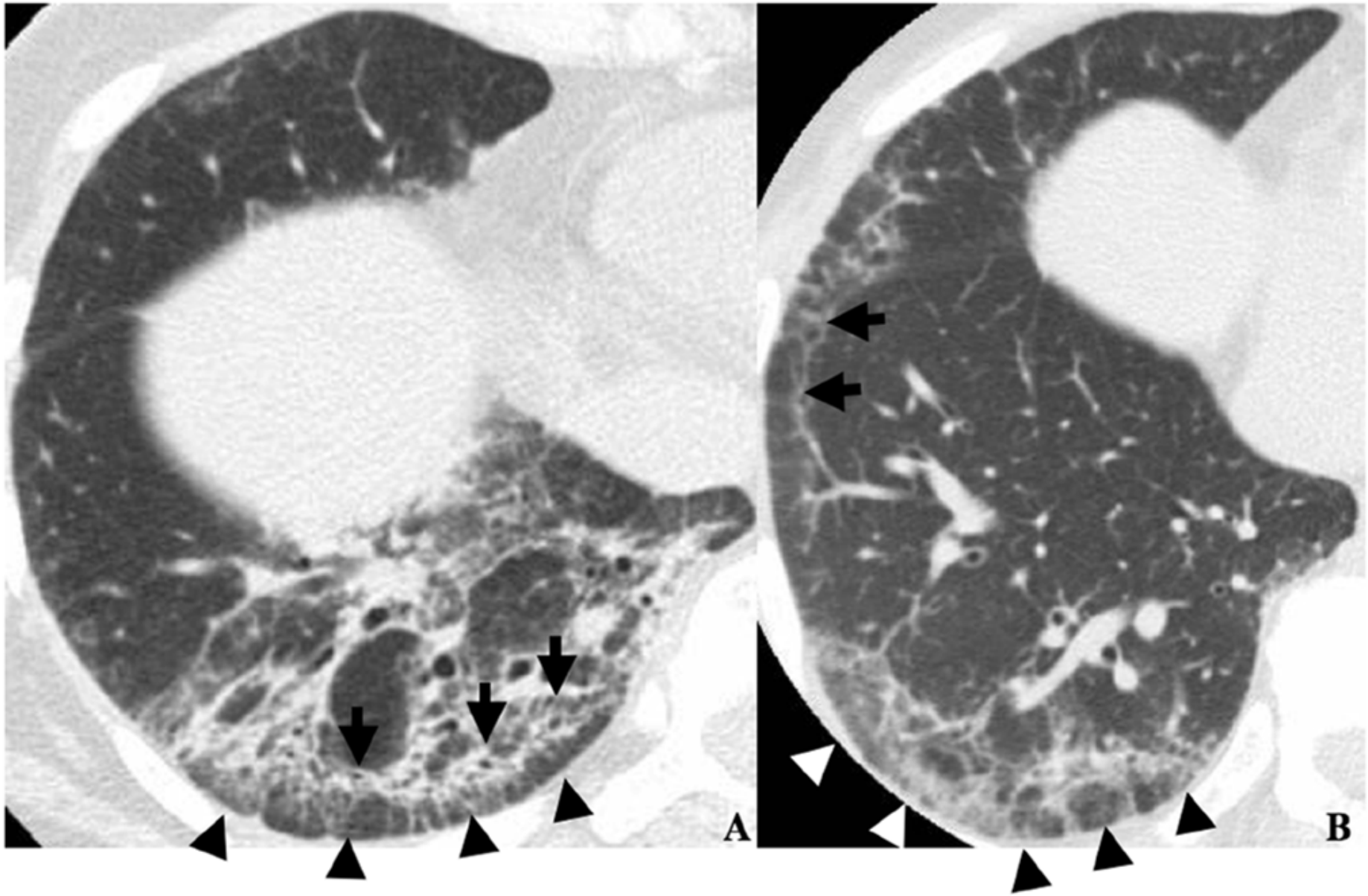
Figure 3. HRCT images showing lower reticulation pattern. A: A 47-year-old woman

negative for anti-CADM-140 (PL-7-positive). Peripheral intralobular reticular opacities with subpleural sparing were the dominant finding (arrowheads). GGAs, interlobular septal thickening, nonseptal linear or plate-like opacities, and traction bronchiectasis (arrows) were also observed. The patient remained alive 6 years after diagnosis. B: A 52-year-old woman negative for anti-CADM-140 (Jo-1-positive). Peripheral intralobular reticular opacities with subpleural sparing were the dominant findings (arrowheads). Interlobular septal thickening and nonseptal linear or plate-like opacities were also prominent (arrows). The patient remained alive 6 years after diagnosis.

Figure 4. HRCT image showing random GGA pattern in a 56-year-old woman positive for anti-CADM-140. Small, peripheral, localized GGAs were distributed in a patchy manner, with no consolidation. The patient remained alive 4 years after diagnosis.






A
B

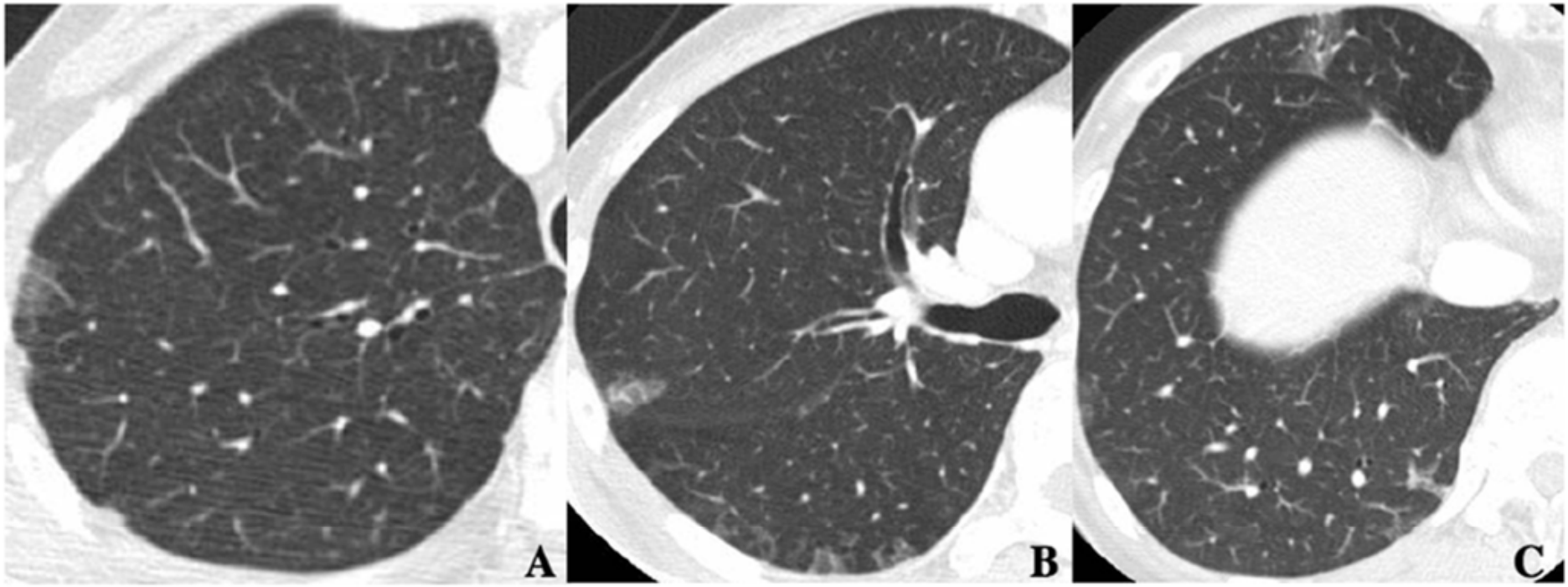

A
B
C

Table 1. Patient demographic, clinical characteristics and laboratory test results at diagnosis

	Anti-CADM-140 (+) (n = 12)				Anti-CADM-140 (-) (n = 13)				*P*
Clinical features									
Sex, male/female	4	/	8		4	/	9		>0.99
Smoking	0		(0.0%)		6		(46.2%)		0.01
Age (years)	53.5	±	9.4		52.7	±	7.7		>0.99
C-ADM at diagnosis	6		(50.0%)		4		(30.8%)		0.43
Acute ILD[*]	3		(25.0%)		0		(0.0%)		0.10
Acute or subacute ILD[§]	5		(41.7%)		1		(7.7%)		0.07
Laboratory tests									
WBC (/mm^3)	5140	±	1390	(n = 12)	8860	±	2940	(n = 13)	<0.01
Plt (×10^4/mm^3)	19.8	±	7.09	(n = 12)	29.9	±	9.38	(n = 13)	<0.01
CRP (mg/dL)	1.03	±	0.84	(n = 12)	1.52	±	1.76	(n = 13)	0.81
LDH (IU/L)	423.2	±	199.4	(n = 12)	429.2	±	161.7	(n = 13)	0.96
CK (IU/L)	261.3	±	314.6	(n = 12)	1348.8	±	1707.0	(n = 13)	<0.01
Aldolase (IU/L)	9.0	±	4.4	(n = 12)	25.1	±	26.5	(n = 13)	0.03
Ferritin (ng/mL)	1267.6	±	2077.3	(n = 10)	196.7	±	252.0	(n = 10)	0.01
Maximal ferritin[†] (ng/mL)	3035.7	±	5253.2	(n = 10)	1575.2	±	4117.5	(n = 10)	0.04
KL-6 (U/mL)	511.8	±	162.3	(n = 12)	907.2	±	750.4	(n = 12)	0.32
SP-D (ng/mL)	44.0	±	20.0	(n = 8)	154.1	±	119.4	(n = 8)	<0.01
Anti ARS antibodies	0		(0.0%)		10		(76.9%)		<0.01

All values are number (percentage) or mean ± standard deviation (number).

*Acute ILD was diagnosed when respiratory failure developed within one month from the onset of symptoms or the initiation of treatment.

§Subacute ILD was diagnosed when respiratory failure developed within one to three months from the onset of symptoms or the initiation of treatment.

†Highest value through the whole course.

Abbreviations: anti-CADM-140, anti-CADM-140 antibody; C-ADM, clinically amyopathic dermatomyositis; ILD, interstitial lung disease, WBC, white blood cell; Plt, platelet; CRP, C-reactive protein; LDH, lactate dehydrogenase; CK, creatine kinase; SP-D, surfactant protein-D; ARS, aminoacyl-tRNA synthetase

Table 2. HRCT findings in anti-CADM-140 (+) and (-) groups

	Anti-CADM-140 (+) (n = 12)		Anti-CADM-140 (-) (n = 13)		*P*
Ground glass attenuation	10	(83.3%)	13	(100.0%)	0.22
Consolidation	7	(58.3%)	6	(46.2%)	0.70
Intralobular reticular opacities	0	(0.0%)	11	(84.6%)	<0.01
Interlobular septal thickening	8	(66.7%)	6	(46.2%)	0.43
Nonseptal linear or plate-like opacities	10	(83.3%)	7	(53.8%)	0.20
Honeycombing	0	(0.0%)	0	(0.0%)	N.A.
Traction bronchiectasis	0	(0.0%)	3	(23.1%)	0.22
Lobular volume loss	5	(41.7%)	7	(53.8%)	0.70
HRCT pattern					
Lower consolidation/GGA	6	(50.0%)	2	(15.4%)	
Lower reticulation	0	(0.0%)	9	(69.2%)	<0.01
Random GGA	4	(33.3%)	0	(0.0%)	
Others‡	2	(16.7%)	2	(15.4%)	

All values are number (percentage).

‡In the anti-CADM-140 (+) group, upper GGA pattern in one and diffuse GGA in another. In the anti-CADM-140 (-) group, lower but axially diffuse GGA pattern in one and diffuse reticulation in another.

Abbreviations: N.A., not available; GGA, ground-glass attenuation

Table 3 Clinical characteristics of 12 anti-CADM-140 positive cases

Case No.	Age	Sex	C-ADM	Acute/subacute ILD	HRCT pattern	Duration‡ (days)	Outcome	Cause of death
1	60	M	-	+	Lower consolidation/GGA	64	Death	Respiratory failure
2	51	M	+	+	Lower consolidation/GGA	87	Death	Respiratory failure
3	44	M	-	+	Lower consolidation/GGA	41	Death	Respiratory failure
4	45	F	+	+	Lower consolidation/GGA	52	Death	Respiratory failure
5	41	F	+	-	Lower consolidation/GGA	97	Survival	
6	52	F	+	-	Lower consolidation/GGA	630	Survival	
7	64	F	+	+	Random GGA	133	Death	Acute exacerbation
8	64	F	-	-	Random GGA	92	Death	PCP, sepsis
9	52	M	−	-	Random GGA	952	Survival	
10	56	F	-	-	Random GGA	1237	Survival	
11	70	F	+	-	Other	122	Death	Respiratory failure
12	43	F	-	-	Other	503	Survival	

‡The follow-up period from the diagnosis

Abbreviations: C-ADM, clinically amyopathic dermatomyositis; ILD, interstitial lung disease; M, male; F, female; GGA, ground-glass attenuation; PCP, *Pneumocystis jiroveci* pneumonia